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A chlorhexidine varnish implemented treatment strategy for chronic periodontitis

Short-term clinical observations

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Abstract

Objectives: The aim of this study was to investigate the clinical outcome of a subgingivally applied chlorhexidine varnish when used as an adjunct to scaling and root planing (SRP) in the treatment of chronic periodontitis.

Material and methods: A randomized controlled, single blind, parallel trial was conducted on the basis of 16 volunteers suffering from chronic periodontitis. The control group received oral hygiene instructions and was scaled and root planed in two sessions. The test group received the same instructions and treatment, however, all pockets were additionally disinfected using a chlorhexidine varnish. The gingival index, plaque index, bleeding on probing, probing pocket depth (PPD) and clinical attachment level (CAL) were recorded at baseline and subsequently after 1 and 3 months.

Results: Both treatment strategies showed significant reductions in PPD and CAL at both follow-up visits by comparison with baseline levels ($p < 0.001$). Yet, at study termination, combination therapy resulted in additional pocket reductions between 0.73 and 1.23 mm ($p < 0.02$), and clinical attachment gains between 0.63 and 1.09 mm ($p < 0.02$).

Conclusions: These findings suggest that a varnish-implemented strategy may improve the clinical outcome for the treatment of chronic periodontitis in comparison with SRP alone.

Key words: chlorhexidine varnish; clinical study; periodontitis; scaling and root planing

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The adequacy of mechanical debridement in the treatment of periodontitis is commonly acknowledged (Badersten et al. 1981, 1984, Hill et al. 1981, Isidor et al. 1984, Ramfjord et al. 1987, Kaldahl et al. 1988). However, scaling and root planing (SRP) was found to be of limited efficacy, especially of deep pockets or furcations because accretions can be easily left behind (Waerhaug 1978, Buchannan & Robertson 1987, Rateitschak-Plüss et al. 1992). Indeed, limited access impedes complete removal of bacterial deposits. Therefore, treatment strategies using antimicrobials in conjunction with SRP have been evolved assuming that chemical aids would compensate for technical shortcomings and furthermore prevent early microbial recolonization to ultimately ensure the best chance for clinical improvements. In spite of the fact that systemic antibiotics have been proven to be effective as an adjunct to SRP (for review, see Herrera et al. 2002), their use should be limited to cases of aggressive periodontitis for obvious reasons of bacterial resistance (van Winkelhoff et al. 2000). Locally-applied antibiotics may require the same caution (Larsen 1991, Goodson & Tanner 1992, Walker et al. 2000). Even though the latter overcomes the non-compliance of the patient (Loesche et al. 1993) and systemic adverse effects, its unfavourable cost–benefit ratio further confines clinical indications (Quirynen et al. 2002). The net clinical effectiveness of topically administered antiseptics as an adjunct to mechanical debridement also remains far from self-evident: subgingival irrigation and gel application were found ineffective (Braatz et al. 1985, MacAlpine et al. 1985, Lander et al. 1986, Oosterwaal et al. 1991, Unsal et al. 1994, Quirynen et al. 2000). Only controlled delivery devices containing chlorhexidine (CHX) (PerioChip™, Perio Products Ltd., Jerusalem, Israel) showed some promise (Soskolne et al. 1997, Jeffcoat et al. 1998), although recent reports could not consolidate any addi-

tive effect (Azmak et al. 2002, Daneshmand et al. 2002, Grisi et al. 2002). Furthermore, these chips are expensive and cost-effectiveness may become unfavourable.

An easy-to-use and affordable vehicle is EC40® (Certichem, Nijmegen, the Netherlands), notably a highly concentrated CHX varnish which can be injected into the periodontal pocket. To date, this varnish was mainly tested for the prevention of caries in high-risk populations. Indeed, by multiply applying EC40® on the tooth surface creating a reservoir of CHX, *Streptococcus mutans* can be suppressed in supragingival plaque, hereby lowering its cariogenic potential (Schaeken et al. 1991, 1994, Ie & Schaeken 1993, Fennis-Ie et al. 1998).

The aim of the present study was to investigate the short-term clinical effect of EC40® when subgingivally applied as an adjunct to SRP in the treatment of moderate-to-severe chronic periodontitis.

Material and Methods

Experimental design

Sixteen systematically healthy patients volunteered for this randomized controlled, single blind, parallel trial. They consulted, or were referred to, the Department of Periodontology of the Free University of Brussels or a private periodontal practice for the treatment of chronic periodontitis. The descriptive statistics of the patients, together with their periodontal status, are summarized in Table 1.

Each volunteer had at least 20 teeth (wisdom teeth excluded) with a minimum of four multi-rooted teeth and four teeth per quadrant. All subjects suffered from moderate-to-severe chronic periodontitis meaning 15% or more of all pockets exhibited a probing pocket depth (PPD) of at least 7 mm, which bled upon probing. Radiographic evidence of extended bone loss ($\geqslant$1/3 of the root length) was also present.

Subjects having taken antibiotics within 4 months prior to or during the trial and those using antiseptics during the trial were excluded. Patients suffering from systemic diseases and/or taking medication likely to induce gingival hypertrophy could not be enrolled according to the study protocol. For obvious reasons of plaque accumulation, subjects wearing removable partial dentures or undergoing orthodontic therapy were excluded. Sites neighbouring recent extraction sockets were systematically excluded, as were teeth showing endodontic–periodontic lesions. If possible, extractions of hopeless teeth were postponed until complete termination of the study. If not, their neighbouring sites were excluded.

After having obtained written informed consent, the participants were randomly assigned to the control group or the test group (eight patients each). Both groups were relatively comparable with respect to gender, age, smoking and degree of periodontal destruction (Table 1). Subjects were considered smokers if they smoked at least 10 cigarettes a day. The Ethical Committee of the University Hospital in Brussels had approved the study protocol.

Treatment

Subjects of the control group received standard periodontal therapy, meaning two-stage SRP using an ultrasonic scaler and standard periodontal curets with a time interval of 1 week between both treatment sessions. In order to synchronize the study, the upper right and lower right quadrant were treated in the first session and the remaining quadrants in the second session. The treated quadrants were polished using a low abrasive paste (Nupro® Fine polishing paste, Ash, Division of Dentsply International Inc., York, UK) and oral hygiene

Table 1. Descriptive statistics of the examined population

Subject	Gender	Smoker*	Age	Mean initial PPD	% of sites with PPD$\geqslant$7 mm and BoP+	% of sites with angular defects†	% of sites with calculus†
Control group							
1	M	–	56	4.59	23	25	38
2	M	–	66	5.01	16	4	44
3	F	–	42	4.82	21	38	59
4	F	–	78	5.08	20	23	93
5	F	+	45	4.28	15	25	25
6	M	–	58	5.13	30	21	31
7	F	–	45	4.48	18	25	2
8	F	–	46	4.21	15	15	66
	Mean		54	4.70	19.75	22	44.75
	Standard deviation		13	0.36	5.06	9.70	27.87
Test group							
1	F	+	58	5.07	23	31	21
2	F	–	32	4.84	18	37	73
3	F	–	60	4.75	20	24	54
4	F	–	39	4.73	19	8	46
5	F	–	54	5.15	26	25	23
6	M	–	36	4.82	20	18	46
7	F	–	51	5.09	30	20	35
8	M	–	34	5.60	32	23	33
	Mean		46	5.01	23.50	23.25	41.38
	Standard deviation		11	0.29	5.29	8.65	17.18
	Independent samples *t*-test (control versus test)		NS	NS	NS	NS	NS

*At least 10 cigarettes a day. †Estimated on intra-oral long-cone radiographs. NS, non-significant at the 5% level of significance; PPD, probing pocket depth; BoP, bleeding on probing.

instructions were given. This included manual brushing and inter-dental plaque control (by using inter-dental brushes or tooth picks). All patients were provided with the same toothpaste (Elmex®, GABA BV, Almere, the Netherlands) and toothbrush (Lactona™, Voprak Lactona BV, Bergen op Zoom, the Netherlands). Oral hygiene was reviewed and, if necessary, re-instructed at the second treatment session and at 1 month.

Subjects of the test group received the same treatment and instructions, however, mechanical debridement was immediately followed by the application of EC40® in all pockets irrespective of the initial PPD using a blunt needle inserted subgingivally and placed into contact with the bottom of the pocket. The varnish was slowly released while the needle was gently moved in a coronal direction. Pockets were deliberately overfilled. The varnish was gently removed 15 min. following its application using a standard periodontal curet. Every tooth was once subjected to EC40® namely immediately following its mechanical debridement during the first or the second treatment session. In order to ensure blindness, one investigator performed SRP and collected all clinical data at baseline, 1 and 3 months, whereas another investigator was charged with the application of the varnish (test group) and all polishing procedures (control and test group).

Adverse effects and the intake of medication were recorded 24 h, 1 week, 1 and 3 months following therapy.

Examination criteria

The following periodontal parameters were recorded in a sequential order by the same investigator at baseline (prior to therapy), 1 and 3 months:

1. The sulcus bleeding index (SBI) (Mühlemann & Son 1971) was measured at six sites (mesial, central, distal; buccally as well as orally) at the Ramfjord teeth (or neighbouring teeth in case of absence). The scores ranged from 0 to 5.
2. The Quigley and Hein plaque index (PI) (1962) was measured at six sites (mesial, central, distal; buccally as well as orally) at the Ramfjord teeth (or neighbouring teeth in case of absence). The scores ranged from 0 to 5.
3. The PPD was measured to the nearest millimeter at six sites per tooth (mesial, central, distal; buccally as well as orally) using a manual probe (CP 15 UNC, Hu-Friedy®, Chicago, FL, USA). The baseline PPD was measured immediately after SRP to avoid interference with calculus deposits.
4. Bleeding on probing (BoP) was evaluated 15 s following pocket probing. A score of 0 (no bleeding) or 1 (bleeding) was given.
5. Location of the gingival margin in relation to the cemento-enamel junction was measured to the nearest millimeter. Recession was given a positive value, whereas pseudo-pockets were given a negative value.
6. The clinical attachment level (CAL) was calculated for each site as the sum of the PPD and the gingival recession or overgrowth.

All recordings were made without access to previous measurements in order to avoid measurement bias.

Calibration session

To ensure reliability of test results, the investigator charged with clinical assessments had to be calibrated for intra-examiner repeatability prior to commencement of the trial. Three patients suffering from chronic periodontitis were enrolled for this purpose. Duplicate measurements ($n = 414$) for PI, PPD and CAL were collected with an interval of 30 min. between the first and the second recording. Scoring was found to be highly reproducible for PI (Spearman's correlation: $r = 0.86$; $p < 0.001$), PPD (Pearson's correlation: $r = 0.92$; $p < 0.001$) and CAL (Pearson's correlation: $r = 0.91$; $p < 0.001$).

Statistical analysis

Data analysis was performed with the subject as the experimental unit. For all periodontal parameters mean values per subject and per visit were calculated. For the gingival index, plaque index and bleeding tendency, a comparison between baseline and one of the follow-up visits was made by means of a paired *t*-test (within-group comparison). Control and test group were compared with each other by using an independent samples *t*-test (between-group comparison). The changes in PPD and CAL over time within each group (within-group comparison) and the impact of the treatment strategy on these parameters (between-group comparison) were examined by means of repeated measures ANOVA with treatment, time and their interaction as fixed effects and the subject as a random effect. A model with the measurements at baseline, month 1 and 3 was used to compare the changes over time in the two treatment groups (interaction effect). Subsequently, the data were split per tooth type (single- *versus* multi-rooted teeth) and initial PPD (medium deep: between 4 and 6 mm PPD; deep: $\geqslant 7$ mm PPD) to allow a site-specific analysis.

Results

Gingival indices and plaque indices

The changes over time in gingival indices and plaque indices are given per treatment strategy in Table 2. At baseline, no statistically significant differences could be found for any of the parameters. Both treatment strategies resulted in similar statistically and clinically significant improvements on the basis of gingival and plaque indices at both follow-up visits when compared with baseline levels. However, the control group showed higher plaque levels than the test group at study termination (2.00 *versus* 1.53; $p = 0.043$).

BoP

The reduction over time in the percentage of sites with BoP is also depicted in

Table 2. Changes in periodontal parameters by treatment strategy

Periodontal parameter	Treatment strategy	Baseline	Month 1	Month 3
Gingival index	Control group	1.12 ± 0.48	$0.43 \pm 0.22^{*}$	$0.27 \pm 0.18^{*}$
(SBI)	Test group	1.25 ± 0.62	$0.30 \pm 0.19^{*}$	$0.33 \pm 0.24^{*}$
Plaque index	Control group	2.66 ± 0.63	$2.01 \pm 0.60^{*}$	$2.00 \pm 0.41^{*}$
(PI)	Test group	2.45 ± 0.52	$1.66 \pm 0.43^{\dagger}$	$1.53 \pm 0.43^{*\ddagger}$
Bleeding on Probing	Control group	70 ± 12	$25 \pm 8^{*}$	$23 \pm 8^{*}$
(BoP%)	Test group	76 ± 9	$21 \pm 5^{*}$	$22 \pm 6^{*}$

Within-group differences:
$^{*}0.005 < p \leqslant 0.05$; $^{\dagger}p \leqslant 0.005$ (between baseline and follow-up visits: paired *t*-test). Between-group differences: $^{\ddagger}0.005 < p \leqslant 0.05$ (between control and test group: independent samples *t*-test).

Table 2. At baseline, study samples were matched with each other. Irrespective of the treatment strategy, bleeding tendency decreased significantly and remained low (<25%). Between-group differences could not be detected at any time.

PPD

Both treatment strategies showed statistically significant reductions in the overall PPD at both follow-up visits when compared with baseline: 1.18 mm for the control group ($p<0.001$), respectively, 2.02 mm for the test group ($p<0.001$) at month 3. Moreover, the additional reduction of 0.84 mm in favour of the test group was highly statistically significant ($p=0.001$). The data were split per tooth type and initial PPD in order to scrutinize inter-group disparities. The changes in PPD over time for each subgroup and tooth type are depicted in Fig. 1. The largest reductions at study termination were obtained for initially deep pockets in both treatment strategies, notably 2.54 mm in the control group *versus* 3.77 mm in the test group pointing to an additional reduction in the test group of 1.23 mm ($p=0.019$). For initially medium deep pockets the additional reduction in favour of the test group was 0.73 mm ($p<0.001$). To emphasize the clinical relevancy of these results, it was shown that the relative amount of pockets within the 0–3 mm PPD range was significantly larger in the test group (74%) than in the control group (61%) ($p=0.004$) at the end of the trial, even though depth distributions were equal at baseline.

CAL

Again, the data were split per tooth type and initial PPD to allow a detailed analysis. The changes in CAL at month 1 and 3, both in relation to baseline, are shown in Fig. 2. Statistically significant clinical attachment gains were systematically recorded for the control group and the test group at both examination points ($p<0.001$). Initially deep pockets encompassed the largest clinical attachment gain at study termination, namely 2.16 mm in the control group *versus* 3.25 mm in the test group. The additive gain of 1.09 mm favouring the test group was highly statistically significant ($p=0.017$). For initially medium deep pockets the additional gain in the test group was 0.63 mm ($p=0.001$).

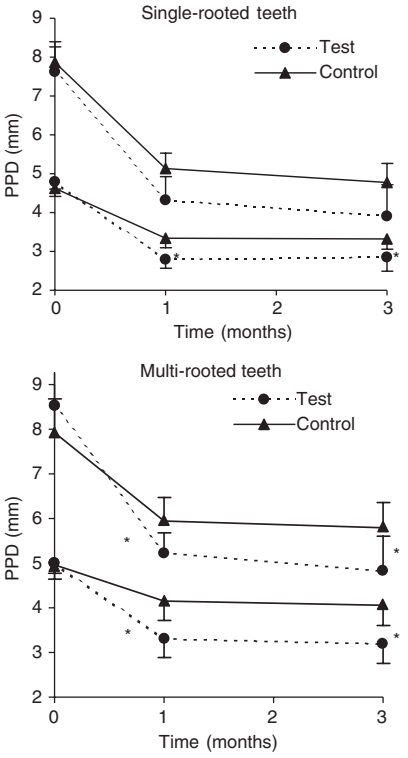

Fig. 1. Changes in probing pocket depth over time for deep (≥7 mm) and medium deep (4–6 mm) pockets. The data are depicted per treatment strategy (control and test) and tooth type (single- and multi-rooted). Between-group differences: $^{*}p\leqslant 0.005$.

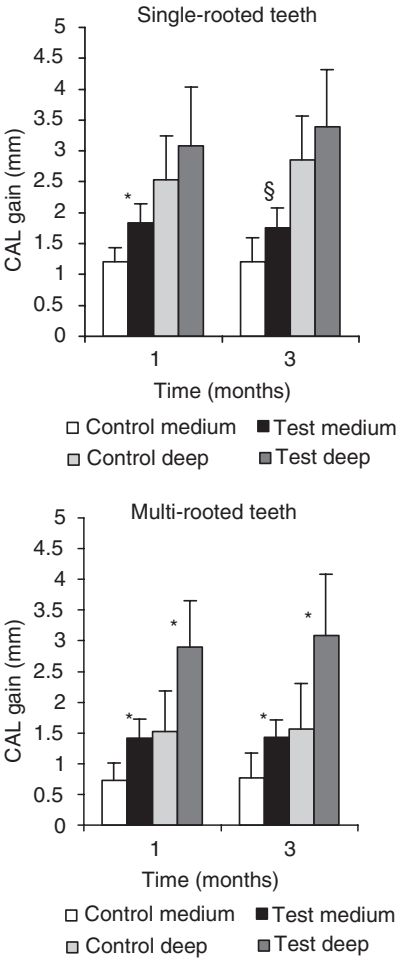

Fig. 2. Changes in clinical attachment level over time for deep (≥7 mm) and medium deep (4–6 mm) pockets. The data are depicted per treatment strategy (control and test) and tooth type (single- and multi-rooted). Between-group differences: § $0.005<p\leqslant 0.05$; $^{*}p\leqslant 0.005$.

Adverse effects

The pain experience after treatment seemed similar in both groups as was the amount of painkillers taken. One subject in the control group expressed clinical signs of recurrent oral ulcerations (ROU) 24 h following therapy. In the test group, one subject informed of taste disturbances. However, this complaint disappeared completely after 2 days. Another volunteer in the test group mentioned light fever during the first day. No important disparities could be noticed between both treatment strategies.

Discussion

The results of this study show that a treatment strategy, supplementing mechanical debridement by subgingival CHX varnish application, provides significantly greater improvements in PPD and CAL compared with those obtained by SRP alone in the treatment of chronic periodontitis. At study termination, combination therapy resulted in additional pocket reductions between 0.73 and 1.23 mm, and additive clinical attachment gains between 0.63 and 1.09 mm.The actual time spent for SRP did not differ significantly between the control and test group (4 min. 44 s on average per tooth for the control group and 4 min. 49 s for the test group; $p>0.05$). The interpretation of these results may require some caution since the plaque levels were considerably lower for the test group (1.66) by comparison with the control group (2.01) at 1 month, even reaching the level of significance at 3 months (1.53 *versus* 2.00; $p=0.043$). This dissimilarity in oral hygiene might have influenced the treatment outcome favouring the test

group especially knowing the experimental groups were small. Yet, it also has to be anticipated that in spite of a dissimilar evolution in plaque levels, gingival levels evolved equally.

Most studies have indicated that initially deep pockets (≥7 mm PPD) reduce in depth by 2 to 2.5 mm as a result of SRP. This reduction is primarily because of an increase in gingival recession by 1 to 1.5 mm. Clinical attachment gain customarily contributes less to this pocket reduction (approximately 1 mm) (Badersten et al. 1981, 1984, Hill et al. 1981, Isidor et al. 1984, Ramfjord et al. 1987, Kaldahl et al. 1988). Deep pockets managed by SRP alone evolved quite differently in our study, exhibiting an increase in gingival recession of only 0.38 mm and gaining clinical attachment of 2.16 mm. This dissimilarity might be a reflection of the following considerations: first, the initial PPD was systematically measured following SRP hereby possibly overrating its real value, concurrently overestimating clinical attachment gain (Claffey et al. 1988). Indeed, a pocket reduction of 2.54 mm was shown for deep pockets of the control group, a value near or even slightly above the upper limit described in the literature. Secondly, gingival recessions might have been underrated hereby further falsely increasing clinical attachment gain. However, if this phenomenon occurred, it cannot explain the difference in treatment outcome between both treatment strategies. Indeed, deep pockets of the test group described a similar deviated course as observed for the control group in terms of clinical attachment gain (3.25 mm) and increase in gingival recession (0.52 mm), consolidating consistent assessments. This observation makes sense knowing high intra-examiner repeatability was reported. Thirdly, we wish to emphasize that this is a pilot study based on a limited sample size making cautiousness imperative when comparing and interpreting results.

Studies dealing with CHX gel application as an adjunct to SRP and its net effect on periodontal conditions remain equivocal: additive effects because of gel administration were found to be negligible (Oosterwaal et al. 1991, Unsal et al. 1994, Quirynen et al. 2000). Yet, our data demonstrate that treatment outcome benefits from a combination approach using a CHX varnish. The disparity between both vehicles and their impact on the periodontal status might be related to a huge difference in CHX concentration (1–2% for the gel *versus* 35% for the varnish). Moreover, it was shown that the expected half-life of a gel within the pocket is about 1 min irrespective of its binding capacity. This extremely fast clearance is explained by a constant outflow of crevicular fluid (Goodson 1989, Oosterwaal et al. 1990). Concurrently, crevicular fluid will promote hardening of the EC40® varnish keeping it much longer within the subgingival area.

With respect to the CHX chip in conjunction with SRP, conclusions on a clinical level remain confusing: mostly, no additional effects were found at 3 months (Jeffcoat et al. 1998, Azmak et al. 2002, Daneshmand et al. 2002, Grisi et al. 2002). Yet, in one multicenter trial an additive pocket reduction of 0.61 mm was described because of insertion of the chip into initially deep pockets (≥7 mm) (Soskolne et al. 1997). The equivalent value of 1.23 mm shown on the basis of our data is clearly higher, although both vehicles contain a comparable amount of CHX (34% for the chip and 35% for the varnish). However, one should keep in mind we recorded initial PPD immediately following SRP hereby possibly overrating values at baseline. Concurrently, initial PPD may have been slightly underrated because of the presence of subgingival calculus deposits in the study by Soskolne et al. (1997), measuring this parameter prior to therapy (Claffey et al. 1988). The higher pocket reduction in our study may also have another explanation: indeed, Soskolne et al. (1997) enrolled 7–8 mm pockets, whereas in this study no upper limit in PPD was set. Furthermore, the total microbial load had to be lower in this study since CHX was administered in all pockets. Apparently, the much higher contact time favouring the chip (7 days for the chip *versus* 15 min. for the varnish) does not seem to be that decisive in altering periodontal conditions. Providing the concentration of CHX incorporated in its vehicle is adjusted, meaning sufficiently high, levels of CHX in the crevicular fluid far above the MIC of 125 μg/mL reported to be inhibitory to 99% of bacteria isolated from pockets will be achieved (Stanley et al. 1989). Hence, bactericidal levels will already be achieved only minutes following administration, substantiating a contact time of 15 min. to be sufficient. Furthermore, a contact time of only 15 min. sets bounds to serious adverse effects. However, local cytotoxic effects and delay of wound healing might be expected when applying these highly concentrated vehicles, even at reduced contact (Helgeland et al. 1971, Kenney et al. 1972, Goldschmidt et al. 1977, Basetti & Kallenberger 1980, Knuutila & Söderling 1981). Yet, these local cytotoxic effects, inducing superficial necrosis of the outer connective tissue layers, might as well serve as a partial explanation for the success of the new treatment strategy: indeed, since some key-periodontopathogens can invade periodontal tissues (Saglie et al. 1982, Allenspach-Petrzilka & Guggenheim 1983), they can be targeted because of this phenomenon.

In 1995, Quirynen and co-workers introduced the ''one-stage full-mouth disinfection'' in the treatment of periodontitis. Several papers have been published proving treatment outcome will benefit from SRP performed within 24 h when compared with quadrant scaling within a time interval of 1–2 weeks (Quirynen et al. 1995, Vandekerckhove et al. 1996, Mongardini et al. 1999). An additional pocket reduction for initially diseased sites between approximately 0.1 and 1.4 mm might be expected because of this one-stage approach (range estimated on the basis of published figures at 3 months follow-up). The treatment strategy using a CHX varnish resulted in comparable additional pocket reductions between 0.73 and 1.23 mm. Although a one-stage approach has its ergonomic advantages, systemic adverse effects because of bacteraemia have been reported (Vandekerckhove et al. 1996). Moreover, in a recent report, sequential scaling has been found to be equally effective as the one-stage full-mouth disinfection, questioning the weight of intra-oral translocation of periodontopathogens in periodontal healing (Apatzidou & Kinane 2004).

The results of this trial in favour of the combination therapy using a highly concentrated CHX varnish seem promising. However, large-scale trials evaluating this concept are necessary to substantiate our results and to determine their clinical relevance at long term. Furthermore, microbiological data specifically assessing the additive effect of the CHX varnish when using it as an adjunct to SRP would be helpful in understanding clinical observations.

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